IN THE ABSTRACT:

Please delete the present Abstract and replace it with the new Abstract attached as new page 185.

REMARKS

Claims 1-28, 30-35, 37-92 and 96-102 remain pending upon entry of the foregoing amendments.

Applicants greatly appreciate the Examiner's careful and thorough review of the claims and the Examiner's helpful suggestions for overcoming the rejections raised.

The claims have been amended to more precisely define the present invention and to correct certain informalities as noted by the Examiner. The Abstract has also been replaced with a shortened version. There being no issues of new matter, entry of the foregoing amendments is respectfully submitted to be proper.

Abstract

The Abstract has been replaced with a new Abstract including the revisions requested by the Examiner.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-35, 37-66, 73, 74, 76, 77, 80, 82, 85-88 and 96 are rejected under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification.

The Examiner argues that the terms "pharmaceutically acceptable" and "therapeutically acceptable" in the claims imply an assertion of in-vivo therapeutic efficacy allegedly not demonstrated in the application.

Applicants respectfully traverse.

The present claims under rejection are directed to compounds and compositions, not methods of treatment (which claims were withdrawn from consideration). In any case, to advance the prosecution, the term "therapeutically acceptable" in claim 96 has been replaced with "pharmaceutically acceptable". The term "pharmaceutically acceptable" in the claims is necessary to define the types of salts, esters, carrier media or auxiliary agents that are covered by the claimed invention, and it is a recognized term of art that simply means "non toxic". Moreover, the specification provides clear guidance as to the pharmaceutically acceptable salts, esters, carrier media or auxiliary agents that can be employed. See, e.g., page 12, line 23 – page 13, line 21, and page 35, line 17 – page 36, line 21.

In addition, Applicants respectfully submit that there is more than adequate evidence in the application as filed that the compounds and compositions of the present invention possess inhibitory activity against the hepatitis C virus and, therefore, would be useful therapeutically to <u>treat</u> a hepatitis C viral infection in-vivo. In this rejection, the Examiner is basically alleging that the claimed compounds and composition do not possess the disclosed utility to treat a hepatitis C viral infection in-vivo (the Examiner's rejection is basically equivalent to making a "lack of utility" rejection under 35 USC § 101). As recently indicated in the "USPTO Training Materials for

Revised Interim Utility Guidelines" (March, 2000; page 4), however, "Since most diseases or conditions can be treated, rejections under 35 USC § 101 [i.e., lack of utility] for treatment claims should rarely be made."

Moreover, the therapeutic utility to treat hepatitis C viral infection in-vivo is just one utility disclosed in the application as filed. With respect to the compound and composition claims, Applicants believe they have met the requirement under 35 USC § 112, first paragraph, for enablement of how to use the claimed invention. The standard test of enablement for compound and composition claims is provided in MPEP §2164.01(c), page 2100-147 second column:

> "In contrast, when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use." (emphasis added)

The same paragraph in discussing multiple uses disclosed in the application then continues:

> "if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention."

Applicants point out that multiple uses are disclosed in the present application. For example, at page 38, lines 17-23, the specification discloses that the compounds of the present invention are also useful as laboratory reagents or to treat or prevent the viral contamination of various materials and, therefore, reduce the risk of viral infection. The data presented in the specification demonstrate that representative compounds within the scope of the invention

exhibit a specific inhibitory effect against hepatitis C virus. This clearly provides evidence of objective enablement for the compound and composition claims with respect to the disclosed utility as a reagent or to treat or prevent the contamination of materials by the hepatitis C virus.

Applicants also point out that if "pharmaceutically acceptable" were deleted from the claims as suggested by the Examiner, leaving only the language "or a salt or ester thereof", the claims would arguably be broader in scope than they are now.

For all the foregoing reasons, Applicants respectfully submit that the present claims are enabled by the application as filed. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-35, 37-66, 73, 74, 76, 77, 80, 82, 85-88 and 96 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

(1) The Examiner refers to the phrase "A is hydroxy or a pharmaceutically acceptable salt or ester thereof" appearing in the 3rd from the last line in claim 1. The Examiner points out that this phrase is redundant because of the phrase "pharmaceutically acceptable salt or ester thereof" in the last line of the claim and is also inaccurate and misleading. In response, claim 1 has been amended so that this phrase only appears in the last line of the claim, as was originally intended. The specification clearly defines what is meant by "pharmaceutically acceptable salts" and "pharmaceutically acceptable esters" at

page 12, line 23 to page 13, line 21. Applicants point out that the definition of "pharmaceutically acceptable esters" at pages 12 to 13 covers compounds where "A, taken together with the carbonyl group to which it is bonded, represents an ester group", as in the Examiner's suggested language. The invention is broader than the language suggested by the Examiner, however, since, as pointed out in the specification, the language "pharmaceutically acceptable esters" covers esterification of <u>any</u> of the carboxyl functions of the molecule. Therefore, Applicants have retained this language at the end of the claim and separate from the A definition itself.

(2) The Examiner alleges that the independent claims are indefinite for failing to recite a functional limitation. Applicants traverse. The independent claims are directed to novel compounds defined by structure. Although these compounds certainly have utility, and can be used as disclosed in the specification, (thus complying with 35 USC §§ 101 and 112), the claimed invention in the independent claims is directed to the <u>compounds per se</u>. These compounds are adequately defined by structure, such that one skilled in the art would clearly understand the scope of the invention. There is no basis in the patent statute or the patent rules for requiring the presence of a functional limitation in a compound claim, where the compound is adequately defined by chemical structure. If the Examiner maintains this requirement, he is respectfully requested to point out where such requirement is found the patent statute or rules.

(3) The Examiner indicates that a claim should be added to mixtures if Applicants intend to claim mixtures of compounds. Applicants' intention in the independent claims is to claim compounds or the optical isomers, diastereoisomers or racemates of the claimed compounds. Of course, by definition, the claimed racemates would constitute mixtures of the opposite optical isomers or diastereoisomers of a single compound. Since the original claim language reciting "including . . ." may have been confusing, Applicants have modified the claim language to conform more closely with Applicants' intention as noted above

(4) Applicants have changed the colon to a semicolon in the R_{2a} definition in claim 1, as suggested by the Examiner.

(5) At the top of page 5, the Examiner noted a grammatical problem with the deletion of "R_{13}, wherein" in claim 23. Applicants intended that "R_{13}, wherein" be deleted in the line following the line identified by the Examiner (the previous Amendment clearly instructed the deletion at Claim 23, line 8, which is the 2nd line under formula (III)). In any case, claim 23 has again been amended in order to resolve this issue

(6) Claims 32 and 63 have been amended as suggested by the Examiner in the middle of

page 5.

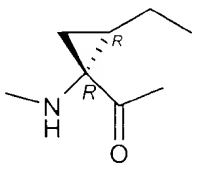
(7) The Examiner indicates that "the P1 segment" in claim 58 lacks antecedent basis in claim 45. In response, claims 58 to 60 have been amended to simply recite "P1".

(8) The misspelling in claim 54 has been corrected.

(9) At the bottom of page 5, the Examiner indicates that claim 59 is drawn to a mixture of compounds whereas the parent claim 45 is drawn to a single compound. Applicants traverse. Claim 59 is drawn to mixtures of diastereoisomers of the same compound, also known as a "racemate" or a "racemic mixture", which is clearly covered by "racemates" in parent claim 45, line 1. The Examiner also alleges that the language "racemic mixture of diastereoisomers" is superfluous and that "diastereoisomers" alone would be sufficient. Applicants do not agree, since "diastereoisomers" alone would not necessarily signify that there is a racemic mixture or racemate, i.e., having no optical activity.

(10) The Examiner requests an explanation of the purpose of the arrows in claims 48, 49, 55, 59, 60, 62 and 66. The purpose of the arrows is to represent the bond by which the substituent is linked to the generic backbone of the compound. For example, if

we were to look at the first structure in claim 66 without the arrows, it could be interpreted as:



whereas it may be confusing what bond is a methyl group and what bond is a linkage to the backbone. Therefore, the arrows are necessary to clearly define the compounds of the invention.

(11) The Examiner points out that "said asymmetric carbon" in claim 61 lacks antecedent basis in claim 58. In response, this language in claim 61 has been replaced with "the C_1 carbon atom", which finds clear support in chemical structure in parent claim 58.

In view of the above, the Examiner is respectfully requested to reconsider and withdraw all the rejections under 35 U.S.C. § 112, second paragraph.

Request for Acknowledgment of IDS

The Examiner is respectfully requested to acknowledge the Information Disclosure Statement filed in this application on May 19, 2000, and return the initialed and signed copies of the PTO-1449 forms with the Examiner's next communication.

Conclusion

In view of the above amendments and remarks, Applicants respectfully submit that this application is now in condition for allowance and earnestly request such action.

If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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